UNIVERSIDADE DE SÃO PAULO
FACULDADE DE ODONTOLOGIA DE BAURU

LUCIANA TREVISAN BITTENCOURT MUNIZ

3D Analysis of the condyle, glenoid fossa and mandible after maxillary protraction anchored in mini implants

Análise tridimensional do côndilo, fossa glenóide e mandíbula após a protração maxilar ancorada em mini implantes

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Orientador: Prof. Dr. Jose Fernando Castanha Henriques

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“Amarei a Luz, pois ela me
mostra o caminho, mas
suportarei as trevas porque ela
me mostra as estrelas”

Og Mandino

ABSTRACT

ABSTRACT

3D Analysis of the condyle, glenoid fossa and mandible after maxillary protraction anchored in mini implants

Introduction: This study aimed to evaluate the three-dimensional condyle, glenoid fossa and mandibular changes after miniscrew-anchored maxillary protraction (MAMP) therapy. **Methods:** The sample comprise 16 patients (7 female; 9 male) with Class III malocclusion and a mean initial age of 10.6 years (SD 1.00). The patients were treated with a mini-implant-supported maxillary protraction therapy using the Hybrid Hyrax appliance and two mandibular miniscrews distally to the permanent canines. Class III elastics were used connecting the maxillary molar hooks to the mandibular mini implants. Three-dimensional analysis was performed using the skull base superimposition of the before and after CBCT. The Paired t and One sample t-tests were used for the interphase comparison. A significance level of 5% was regarded for all tests. **Results:** No intragroup statistical difference was found in the three spatial planes after treatment for glenoid fossa and condyle. An increase in mandibular plane angulation and gonial angle was observed after treatment with MAMP therapy. The mandibular incisors showed a slight labial tip after treatment. Regarding the mandibular landmarks displacements, only the Gnathion showed a backward and downward change with treatment. **Conclusion:** The right and left condylion, right and left anterior fossa, right and left articular eminence showed similar and slight displacements in all planes of space after MAMP therapy. Slight changes were observed in the mandible after treatment with MAMP therapy. A clockwise rotation of the mandibular plane was observed. A slight posterior and inferior displacement of the anterior region of mandibular symphysis was observed after MAMP.

Keywords: Orthodontics, Interceptive; Malocclusion, Angle Class III; Palatal expansion technique.

RESUMO

RESUMO

Análise tridimensional do côndilo, fossa glenóide e mandíbula após a protração maxilar ancorada em mini implantes

Introdução: Este estudo teve como objetivo avaliar as alterações tridimensionais do côndilo, fossa glenoide e mandíbula após a terapia de protração maxilar ancorada com mini-implantes (MAMP). **Métodos:** A amostra é composta por 16 pacientes (7 do sexo feminino; 9 do sexo masculino) com má oclusão de Classe III e idade inicial média de 10,6 anos (DP 1,00). Os pacientes foram tratados com uma terapia de protração maxilar suportada por mini-implante usando o aparelho Hybrid Hyrax e dois mini-implantes mandibulares distalmente aos caninos permanentes. Elásticos classe III foram usados conectando os ganchos dos molares superiores aos mini-implantes inferiores. A análise tridimensional foi realizada usando a sobreposição da base do crânio do antes e depois da TCFC. Os testes t emparelhados e de uma amostra foram usados para a comparação entre as fases. Foi considerado um nível de significância de 5% para todos os testes. **Resultados:** Não foi encontrada diferença estatística intragrupo nos três planos espaciais após tratamento para fossa glenoide e côndilo. Um aumento na angulação do plano mandibular e ângulo goníaco foi observado após o tratamento com terapia MAMP. Os incisivos inferiores mostraram uma ligeira ponta labial após o tratamento. Em relação aos deslocamentos dos pontos mandibulares, apenas o Gnátio apresentou mudança para trás e para baixo com o tratamento. **Conclusão:** Os côndilos direito e esquerdo, fossa anterior direita e esquerda, eminência articular direita e esquerda apresentaram deslocamentos semelhantes e leves em todos os planos do espaço após a terapia com MAMP. Pequenas alterações foram observadas na mandíbula após o tratamento com a terapia com MAMP. Foi observada uma rotação no sentido horário do plano mandibular. Um leve deslocamento posterior e inferior da região anterior da sínfise mandibular foi observado após MAMP.

Palavras-chave: Ortodontia Interceptativa, Maloclusão, Classe III de Angle, Expansão palatina.

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LIST OF ABREVIATIONS AND ACRONYMS

S	Sella
N	Nasion
B	B-point
Co	Condylion
Go	Gonion
Gn	Gnathion
II	Incisor
RCo	Right Condyle
LCo	Left Condyle
RMP	Right Medial Pole
RDP	Right Distal Pole
LMP	Left Medial Pole
LDP	Left Distal Pole
RAF	Right Articular Fossa
LAF	Left Articular Fossa
RAE	Right Articular Eminence
LAE	Left Articular Eminence

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1 INTRODUCTION

1 INTRODUCTION

Class III malocclusion is one of the most challenging and perplexing orthodontics treatments, mainly because of the uncertainty of a stable outcome after the active growth period. The clinical success of Class III treatment in most patients through growth modification, however, has resulted in the development of several strategies to treat Class III disharmony.[1-3] Facemask is usually used in early permanent dentition therapy and allow a downward and forward movement of the maxilla with slight counterclockwise rotation of the palatal plane, and in the mandible, promote an increase of the anteriorinfeior height face, with a minimal dental effects.[4] In the early permanent dentition, we have a recent new treatment using miniscrews as anchorage, that allow us to apply forces on the bone, with minimum dental effects.[5]

Late treatment initiation in the BAMP protocol (maxillary advancement induced by maxillary protraction with bone anchorage) leads to a shorter total treatment time due to a shorter interval between Phase I and Phase II treatments. Upon completion of this therapy, patients are ready to begin comprehensive orthodontics. In addition, it may allow patients who have not been seen at an earlier age for orthodontic treatment or who have not been successfully treated with a face mask to be treated by orthodontists at a later age.[6]

The changes promoted in the temporomandibular joint (TMJ) after Class III treatment has been very controversial in the literature.[1,2] The chin is often an anchorage region for Class III treatment which results in a clockwise rotation force applied directly to the mandible. The mandible may be displaced downward and backward during treatment and the mandibular angle plane increase.[3] The posterior displacement of the condyle and anterior displacement of the articular disc can be considered risks for Class III treatment.[4,5]

Patients treated with BAMP therapy showed significant mandibular changes, although to a lesser degree with regard to maxillary changes. Condyle posterior displacement and anteriorly reoriented direction of condyle growth. The combination of changes resulted in a marked improvement in intermaxillary relationships. Significant albeit small rotation (about 1°) in the clockwise direction of the palatal plane and counterclockwise rotation of the mandibular plane. A significant upward direction of condylar growth was assessed in the treated group compared to the untreated control (Co-Go-Me, about 4°).[7] In another study, in the BAMP treatment protocol, the mandibular line showed significantly different rotation in relation to the cranial base and the nasal line in patients, compared to patients with ERM / FM counterclockwise rotation compared to rotation in the clockwise with the face mask). These differences in the rotational response of the mandible can also affect the sagittal position of the mandible.[6]

In early permanent dentition, Class III growing patients treated with miniscrew-anchored maxillary protraction (MAMP therapy) showed a favorable change in the skeletal and dental sagittal relationships with an adequate vertical control.[8] This treatment showed a great overjet correction when associated with a hybrid hyrax (with 94,4%) and with conventional hyrax (71,4%); with a difference that the group treated with hybrid hyrax promoted greater control of the mesial displacement of maxillary first molar.[9]

No previous studies have evaluated the 3D mandibular changes after MAMP therapy. The objective of this study was to evaluate the three-dimensional condyle, glenoid fossa and mandibular changes after miniscrew maxillary protraction therapy. The hypothesis was that no significant mandibular changes is observed after MAMP therapy.

2 ARTICLES

2 ARTICLES

2.1 ARTICLE 1 - MANDIBULAR CHANGES AFTER MINISCREW-ANCHORED MAXILLARY PROTRACTION: A 3D ANALYSIS

The article presented in this Dissertation was written according to the American Journal of Orthodontics and Dentofacial Orthopedics instructions and guidelines for article submission.

MANDIBULAR CHANGES AFTER MINISCREW-ANCHORED MAXILLARY PROTRACTION: A 3D ANALYSIS

Abstract

Introduction: This study aimed to evaluate the three-dimensional mandibular changes after miniscrew-anchored maxillary protraction (MAMP) therapy. **Methods:** The sample comprise 16 patients (7 female; 9 male) with Class III malocclusion and a mean initial age of 10.6 years (SD 1.00). The patients were treated with a mini-implant-supported maxillary protraction therapy using the Hybrid Hyrax appliance and two mandibular miniscrews distally to the permanent canines. Class III elastics were used connecting the maxillary molar hooks to the mandibular mini implants. Three-dimensional analysis was performed using the skull base superimposition of the before and after CBCT. The Paired t and One sample t-tests were used for the interphase comparison. A significance level of 5% was regarded for all tests. **Results:** An increase in mandibular plane angulation and gonial angle was observed after treatment with MAMP therapy. The mandibular incisors showed a slight labial tip after treatment. Regarding the mandibular landmarks displacements, only the Gnathion showed a backward and downward change with treatment. **Conclusion:** Slight changes were observed in the mandible after treatment with MAMP therapy. A clockwise rotation of the mandibular plane was observed. A slight posterior and inferior displacement of the anterior region of mandibular symphysis was observed after MAMP.

Introduction

Class III malocclusion is one of the most challenging and perplexing orthodontics treatments, mainly because of the uncertainty of a stable outcome after the active growth period. The clinical success of Class III treatment in most patients through growth modification, however, has resulted in the development of several strategies to treat Class III disharmony.[1-3] Facemask is usually used in early permanent dentition therapy and allow a downward and forward movement of the maxilla with slight counterclockwise rotation of the palatal plane, and in the mandible, promote an increase of the anteriorinfeior height face, with a minimal dental effects.[4] In the early permanent dentition, we have a recent new treatment using miniscrews as anchorage, that allow us to apply forces on the bone, with minimum dental effects.[5]

Late treatment initiation in the BAMP protocol (maxillary advancement induced by maxillary protraction with bone anchorage) leads to a shorter total treatment time due to a shorter interval between Phase I and Phase II treatments. Upon completion of this therapy, patients are ready to begin comprehensive orthodontics. In addition, it may allow patients who have not been seen at an earlier age for orthodontic treatment or who have not been successfully treated with a face mask to be treated by orthodontists at a later age.[6] Patients treated with BAMP therapy showed significant mandibular changes, although to a lesser degree with regard to maxillary changes. Condyle posterior displacement and anteriorly reoriented direction of condyle growth. The combination of changes resulted in a marked improvement in intermaxillary relationships. Significant albeit small rotation (about 1°) in the clockwise direction of the palatal plane and counterclockwise rotation of the mandibular plane. A significant upward direction of condylar growth was assessed in the treated group compared to the untreated control (Co-Go-Me, about 4°).[7] In another study, in the BAMP treatment protocol, the mandibular line showed significantly different rotation in relation to the cranial base and the nasal line in patients, compared to patients with ERM / FM counterclockwise rotation compared to rotation in the clockwise with the face mask). These differences in the rotational response of the mandible can also affect the sagittal position of the mandible.[6]

In early permanent dentition, Class III growing patients treated with miniscrew-anchored maxillary protraction (MAMP therapy) showed a favorable change in the skeletal and dental sagittal relationships with an adequate vertical control.[8] This treatment showed a great overjet correction when associated with a hybrid hyrax (with 94,4%) and with conventional hyrax (71,4%); with a difference that the group treated with hybrid hyrax promoted greater control of the mesial displacement of maxillary first molar.[9]

No previous studies have evaluated the 3D mandibular changes after MAMP therapy. The objective of this study was to evaluate the three-dimensional mandibular changes after miniscrew maxillary protraction therapy. The hypothesis was that no significant mandibular changes is observed after MAMP therapy.

Material and Methods

Sample

The sample of this study was obtained from a previous randomized clinical trial.[9] The sample was composed of 16 patients (9 male, 7 female) with a mean initial age of 10.6 years (SD 1.00). The patients were treated at the Orthodontic clinic of Bauru Dental School, University of São Paulo, from July 2017 to June 2019 by a single orthodontist.

The sample calculation was performed considering a standard deviation of 0.9310 in the variable Right Condyle Posterior Surface[10] and a minimum difference to be detected of 1.0 mm. For a power of 80% and 5% of alpha error, 13 individuals were need. The initial sample consisted of 18 individuals. Two patients were excluded for presenting an open mouth in the CBCT exam.

The inclusion criteria were: (1) patients of both sexes; (2) between 9 and 13 years of age in the late mixed or early permanent dentition; (3) Class III skeletal malocclusion (Wits appraisal equal to or less than -1mm). The exclusion criteria were: (1) patients with unerupted mandibular canines; (2) patients with a history of orthodontic treatment; (3) patients with systemic or neurological alterations.

Patients treated with mini-implant-supported maxillary protraction therapy (MAMP) using the Hybrid Hyrax appliance. In the maxillary arch, a prefabricated hybrid hyrax was installed using the third palatal wrinkle as a reference. Two palatal mini-implants measuring 1.8 mm in diameter, 7 mm in length and 4 mm transmucosal (PecLab, Belo Horizonte, Brazil) were positioned after local anesthesia, using an implant motor with 35Ncm and 30 revolutions per minute. In the lower arch, two mini-implants measuring 1.6 mm in diameter, 6 mm in length and 1 mm of transmucosal (PecLab, Belo Horizonte, Brazil). Parents were instructed to activate the Hybrid expander for 14 days, one return in the morning and one return in the evening, resulting in a total of 7mm of activation.

Two miniscrews were positioned distally to the permanent mandibular canines, after local infiltration anesthesia and using the line mucogingival as a reference. Full time Class III elastics were used connecting the maxillary molar hooks to the mandibular mini implants for an average of 11.8 months (SD 3.9). Class III elastic force was initiated with 150 g reaching 250g force in the second month.

Cone-beam computed tomography exams were obtained before and after treatment using i-CAT 3D System (Imaging Sciences, Hartfield PA, USA) with a work regime of 120 kVp, 8 mA, 0.25mm voxel size and an examination time of 26.9 seconds.

Image Analysis

Three-dimensional analysis was performed using SlicerCMF (version 4.0; http:// www.slicer.org). The original tomography files were in DICOM format and are converted into “gipl.gz” files using the open ITK-SNAP software, from which the 3D image analysis was performed:

1.Segmentation: construction of a volumetric label 11 of the initial tomography (T1) of the skull base, maxilla and/or mandible, using the ITK-SNAP12 software (http://www.itksnap.org).

2. Head orientation:[11] In the surface models generated in the Slicer.

3. Overlapping the initial tomography (T1) with the final tomography (T2). CT scans are approximate with reference to the base of the skull using the Slicer software transformation tool.

4. Construction of a 3D mask for the cranial base registration superimposition using ITK snap.

5. Skull base image registration:15 Automatic method of image registration based on voxels16 using Slicer software. This method uses a segmentation like a mask of a stable region of the base of the skull to guide the corresponding voxels that are compatible with the image. A matrix is generated from this step and applied to T2 at the cephalometric points so that they become corresponding to T1 and can thus be superimposed.

5. Place the cephalometric points at T1 and T2:14 in the ITK-SNAP software (Fig 2C), these points will be placed on the base of the skull and mandible.

6. Generate the 3D models in 3D Slicer.

7. Landmarks on Q3DC: Slicer software tool for quantitative assessments from the cephalometric points to be studied. Calculation of the distances between the points of

T1 and T2 regardless of the image recording at the base of the skull, differences between the images are evaluated by subtracting the two separate measurements for each treatment time. Calculation of the distances between points T1 and T2 using the image record at the base of the skull. Using the overlapping methods, changes occurring between two treatment times can be measured and quantified by the difference in the overlapping of cephalometric points that had already been selected.

8. Generation of semitranparent overlays and malor maps for visualization.

Reliability and reproducibility of the image analysis registration[11-15] and quantitative methods using the Q3DC tool[12,16,17] have been verified with previously published literature.

Measurements were organized into angular (in degrees) and linear (in millimeters) changes for all three superimpositions.

Statistical Analysis

All measurements were performed by a single observer. Descriptive statistics included the mean and SD of 3D landmark displacements from T1 to T2. Interphase changes were evaluated using 1-sample t tests ($p<0.05$). The statistical analyses were calculated using Statistica (Statistica for Windows, version 7.0, Copyright StatSoft, Inc, Tulsa, Oklahoma, EUA, 2005). One sample t-tests were conducted based on the mean difference between T1 values and T2 values, in order to show the effectiveness of the treatment modality. The comparative mean value for the one sample t-test was 0.0, as defined in the study’s null hypothesis. Several results found a statistical significance when compared to 0.0 or no change; however, for some of these measurements the findings may not be clinically relevant.

Results

The length and anteroposterior position of the mandible remained stable during treatment (CoGn and SNB, table II). The mandibular plane angulation increased by 2^{o} after treatment (Table II). The gonial angle (CoGo.GoGn) showed a slight but significant increase after treatment (+0.6^{o}). A slight labial tip of the mandibular incisor was also observed (II.GoGn) as shown in Table II. The vertical position of the mandibular incisors relative to Gn was not changed during treatment (Table II).

All mandibular landmarks demonstrated a significant 3D displacement after MAMP therapy (Table III). However, only Gnathion showed a significant anteroposterior and vertical displacement from T1 to T2 (Table III). Gnathion moved backward (-0.54mm) and downward (-0.31mm) with treatment (Table III).

Discussion

No previous studies have evaluated the 3D mandibular changes after MAMP therapy. Three-dimensional methods permit to superimpose dental records to visualize treatment effects, eliminating potential downsides of two-dimensional records such as patient head positioning.[11] In this study, the three-dimensional displacement of the mandible relative to the cranial base was assessed. Our study used a standardized method of superimposing three-dimensional data previously validated and used in other studies.[12-15,18,19]

The length and the anteroposterior position of the mandible remained stable during treatment (CoGn and SNB, table II). Previous cephalometric studies of MAMP therapy have also observed that the anteroposterior position of the mandible remained stable after treatment.[8,9] On the other hand, BAMP therapy produced a slightly decrease of the SNB angle generating a small retrusion of the chin after the therapy. The chin retrusion occurred due to bone remodeling of the glenoid fossa toward posterior and due the closure of the mandible , gonial angle after BAMP therapy.[6,20] The anteroposterior displacement of Gn landmark (Table III) demonstrated a slight posterior displacement of the symphysis after MAMP therapy that was not considered clinically relevant. Although, MAMP and BAMP use Class III elastics as the active force, the direction of the force is slightly different between these therapies. In MAMP therapy, the Class III elastics are more horizontal compared to BAMP because the application point in the maxillary arch is the first molar bands. In BAMP therapy, the application point in the maxilla is approximately at the level of mucogengival junction of molars. The difference in force direction might explain the differences in the mandibular outcomes found in this study.

The Sn.GoGn angle increased by two degrees after MAMP therapy (Table IIA slight but significant increase (+0.6º) in the gonial angle (CoGo.GoGn) was also observed in our study. In addition. the Gn landmark slightly displaced downward (-0.3MM) in the SI component (Table III), following the tendency of those planes.

In a previous study using MAMP therapy from Miranda *et al*[9], what they could observe was that the mandibular plane rotating back and downward, results that were similar to facemask therapy that produced a clockwise rotation of the mandibular plane. These findings are in agreement with this study that we could observe an increase of 0.61MM, statistically significant, on the time two (Table II). Studies with BAMP showed that this therapy produced a counterclockwise rotation of the mandible. [20] The differences between MAMP and BAMP might be explained by the direction of the Class III elastics. In the BAMP therapy, the Class III elastics has a greater vertical component of force that acting at the anterior region of the mandible produce a gonial angle closure and a upward rotation of the mandibular plane.[20] In addition, in BAMP therapy, the Class III elastic force is positioned more anteriorly in the mandibular body compared to MAMP. The downward rotation of the mandible in MAMP therapy contributed to maintain stable the sagittal position of the symphysis during treatment.

A slight labial tip of the mandibular incisor (II.GoGn) was found after MAMP therapy. The improvement in the maxillomandibular relationship and the correction of the negative overjet might explain the mandibular incisor labial movement. These findings are in agreement with mandibular incisor proclination observed after BAMP therapy.[7] On the other hand, the mandibular molars showed a 3D displacement similar to the mandible that means no dental effect was observed in mandibular posterior teeth once only skeletal anchorage was used during MAMP therapy.

The results from this study are limited to a short-term observation period immediately after active treatment. Future studies are necessary to evaluate the long-term stability of MAMP outcomes.

Conclusion

Mandibular plane rotated clockwise after MAMP therapy. The anterior region of the mandibular symphysis slightly displaced toward posterior and inferior. The mandibular length remained stable during treatment.

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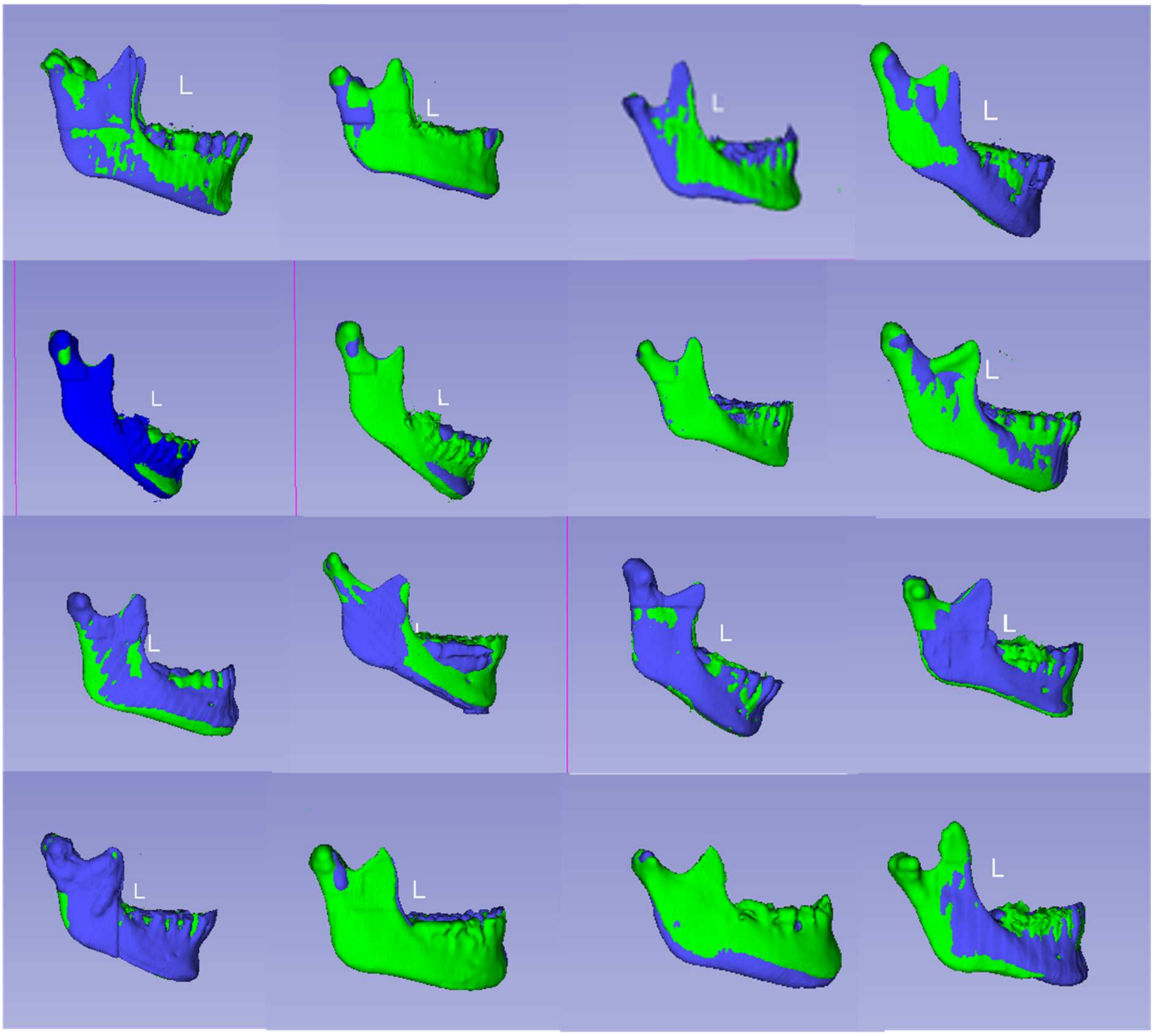

Fig. 1 Lareral visualization of the semitransparency superimposition of T1 (green) and T2 (blue) mandibles.

Table I. Landmarks definition.

S	Sella	The most central point of sella turcica from supero-inferior, antero-posterior, and transversal aspects.
N	Nasion	Most antero-superior junction of frontonasal suture.
B	B-point	Deepest concavity near the transversal midline at the anterior mandible (between incisors and Pog).
Co	Condylion	Two points placed (right and left Condylion) on most lateral posterior superior point of head of condyle. Midpoint taken between two points.
Go	Gonion	Two points placed (right and left Gonion) on most lateral posterior inferior point at angle of mandible, constructed point perpendicular to bisection of ramus of mandible and mandibular plane. Midpoint taken between two points.
Gn	Gnathion	Point on anterior mandibular symphysis centered from postero-superior and transversal aspects and constructed perpendicular to midway point between Pogonion and Menton.
II	Incisor	Center (mesio-distal and bucco-lingual aspects) of the incisal edge of the most proclined mandibular central incisor (if both incisors similar in inclination, the mandibular right central incisor used). The most apical point of the root apex of the most proclined mandibular central incisor (if both incisors similar in inclination, the mandibular right central incisor used).
Note: All landmarks were placed while being viewed in all three planes of space. Note: All landmarks were placed using the same cross-sectional view for standardization.		

Table II. Changes in angular and linear measurements with treatment (Paired T-test).

Variable	**T1** Mean (SD)	**T2** Mean (SD)	**T2-T1** Mean	**95% CI** Lower,Upper	**P value***
Angular					
SNB	87.14 (6.84)	86.91 (5.54)	-0.22	-2.40, 1.96	0.832+
SN.GoGn	29.37 (8.09)	31.48 (6.59)	2.11	0.31, 3.9	0.025*+
CoGo.GoGn	63.20 (5.48)	63.82 (5.41)	0.61	-0.97, -0.26	0.002*+
II.GoGn	100.55 (3.08)	101.50 (3.22)	0.94	-1.45, -0.44	0.001*+
Linear					
II-Gn	29.32 (1.70)	29.05 (2.04)	0.19	-0.59, 1.00	0.464++
Co-Gn	103.15 (7.11)	102.79 (6.49)	0.16	-0.54, 1.27	0.605++

*Statistically significant at P<0.05. ; + Paired t test; ++ Wilcoxon test

Table III. Three-dimensional, anteroposterior (AP) and superoinferior (SI) displacements (mm) with treatment (One Sample T-test)

Variable	Measurement	Mean	SD	95% CI Lower, Upper	P value*
Co	*AP*	0.18	0.74	-0.20, 0.58	0.328 +
	SI	0.12	0.81	-0.30, 0.56	0.548 +
	3D	0.93	0.50	0.66, 1.20	< .001* +
B	*AP*	-0.42	1.20	-1.06, 0.21	0.177 +
	SI	0.14	0.34	0.32, 0.03	0.109 +
	3D	1.25	0.48	0.99, 1.51	< .001* +
Gn	*AP*	-0.54	0.96	-1.05, -0.03	0.039* +
	SI	-0.31	0.58	0.62, -0.00	0.047* +
	3D	1.22	0.54	0.94, 1.51	< .001* +
II	*AP*	0.30	0.68	-0.06, 0.81	0.056 ++
	SI	0.03	0.60	-0.29, 0.35	0.844 +
	3D	0.44	0.29	0.28, 0.59	< .001* +
L6	*AP*	-0.36	1.13	-1.01, 0.32	0.348 ++
	SI	-0.14	0.34	-0.32, 0.03	0.109 +
	3D	1.19	0.43	0.96, 1.42	< .001* +

*Statistically significant at P<0.05; + One Sample T-test; ++ Wilcoxon W

2.2 ARTICLE 2 - CONDYLE AND GLENOID FOSSA 3D-CHANGES AFTER MINI-SCREW ANCHORED MAXILLARY PROTRACTION

The article presented in this Dissertation was written according to the American Journal of Orthodontics and Dentofacial Orthopedics instructions and guidelines for article submission.

CONDYLE AND GLENOID FOSSA 3D-CHANGES AFTER MINI-SCREW ANCHORED MAXILLARY PROTRACTION

Abstract

Introduction: This study aimed to evaluate the three-dimensional condyle and glenoid fossa changes after miniscrew-anchored maxillary protraction (MAMP) therapy. **Methods:** The sample comprise 16 patients (7 female and 9 male) with Class III malocclusion and a mean initial age of 10.6 years (SD 1.00m). The patients were treated with the miniscrew-anchored maxillary protraction therapy using a Hybrid Hyrax expander and two mandibular miniscrews distally to the permanent canines. Class III elastics were used connecting the maxillary molar hooks to the mandibular miniscrews. The total treatment time was 11.3 months. Three-dimensional analysis of the condyle remodeling and glenoid fossa changes were performed using cranial base superimposition of the images of cone-beam computed tomography acquired before and after the therapy. The one sample t-test was used for the interphase comparison ($p<0.05$). **Results**: The right and left condyles show an AP measurement (-0.47;0.05); the SI movement (0.89; 1.44); and in the 3D measurement (2.56; 2.85). The right and left articular fossa, the AP movements (0.21; 0.28); SI movements (-0.45; 0.06); 3D movement (1.86;1.65). On the right and left articular eminence, the AP movement (0.12; 0.13); for SI (-0.15; 0.12); 3D component (1.37; 1.09). **Conclusion:** The MAMP therapy no produced significantly 3D displacement in the patients treated regardless of the direction of the 3D changes: anteroposterior, superior-inferior and 3D movements. Condyle show a little movement up; articular fossa little movement forward and the articular eminence movement up and forward.

Introduction

The changes promoted in the temporomandibular joint (TMJ) after Class III treatment has been very controversial in the literature.[1,2] The chin is often an anchorage region for Class III treatment which results in a clockwise rotation force applied directly to the mandible. The mandible may be displaced downward and backward during treatment and the mandibular angle plane increase.[3] The posterior displacement of the condyle and anterior displacement of the articular disc can be considered risks for Class III treatment.[4,5]

Three-dimensional imaging makes it possible to visualize the modeling processes in the glenoid fossae and condyles.[7] Previous three-dimensional studies showed that facemask therapy lead to bone apposition at the anterior eminence of the TMJ and bone resorption at the posterior wall of the articular eminence, with correlated well with the posterior displacement of the condyle.[6,7] Three-dimensional assessments also showed the bone-anchored maxillary protraction (BAMP) therapy effects on the condyle and glenoid fossa.[7] Significant mandibular changes, although with a lesser degree with regard to maxillary changes, were observed.[7,8] A condyle posterior displacement and anteriorly reoriented direction of condyle growth occurred in the treatment group.[7] A great correlation between remodeling of the anterior and posterior eminences of the glenoid fossa and displacement of the opposing condylar surfaces was observed.[7]

Miniscrew-anchored maxillary protraction (MAMP) therapy was recently described to treat Class III patients in the early permanent dentition.[9,10] The hybrid expander with 2 miniscrews in the maxilla and 2 miniscrews in the anterior region of the mandible were associated with full-time Class III elastics. The overjet correction was achieved in 94,4% of the patients.[9] MAMP also produced favorable changes in dental and skeletal sagittal relationships.[9,10] Although MAMP therapy insert full time posterior and superior force against temporomandibular joints, no previous studies have evaluated the effect of MAMP on the condyle and glenoid fossa changes.

The objective of this study was to evaluate the condyle remodeling and glenoid fossa changes after miniscrew anchored maxillary protraction in growing patients. The null hypothesis was that no significant changes are observed in the temporomandibular joint after MAMP therapy.

Material and Methods

Sample

The sample of this study was obtained from a previous randomized clinical trial.[9] The sample was composed of 16 patients (7 female and 9 male) with a mean initial age of 10.6 years (SD 1.00m). The patients were treated at the Orthodontic clinic of Bauru Dental School, University of São Paulo, from July 2017 to June 2019 by a single orthodontist. This study was approved by the Ethical Committee of Bauru Dental School, University of São Paulo (CAAE: 57981622.2.0000.5417).

The sample calculation was performed considering a standard deviation of 0.93 for the variable Right Condyle Posterior Surface[11] and a minimum difference to be detected of 1.0 mm. For a power of 80% and alpha error of 5%, 13 individuals were needed.

The inclusion criteria were: (1) patients of both sexes; (2) between 9 and 13 years of age in the late mixed or early permanent dentition; (3) Class III skeletal malocclusion (Wits appraisal equal to or less than -1mm). The exclusion criteria were: (1) patients with unerupted mandibular canines; (2) patients with a history of orthodontic treatment; (3) patients with systemic or neurological alterations.

Patients were treated with miniscrew-anchored maxillary protraction therapy (MAMP). In the maxillary arch, a prefabricated hybrid hyrax was installed using the third palatal rugae as reference. Two palatal miniscrew measuring 1.8 mm in diameter, 7 mm in length and 4 mm transmucosal (PecLab, Belo Horizonte, Brazil) were positioned after local anesthesia, using an implant motor driver with 35Ncm and 30 rotations per minute. In the mandible, two miniscrews measuring 1.6 mm in diameter, 6 mm in length and 1 mm of transmucosal (PecLab, Belo Horizonte, Brazil) were placed distally to the permanent canines and using the line mucogingival as a reference.

Parents were instructed to activate the expander for 14 days, 1/4 turn in the morning and 1/4 turn in the evening, resulting in a total of 5.6 mm of activation. Full time Class III elastics were used connecting the maxillary molar hooks to the mandibular miniscrews for an average of 11.3 months. Class III elastic force was initiated with 150g, reaching 250g force in the following months.

Cone-beam computed tomography (CBCT) exams were obtained before and after treatment using i-CAT 3D System (Imaging Sciences, Hartfield PA, USA) with a work regime of 120 kVp, 8 mA, 0.25mm voxel size and an examination time of 26.9 seconds.

Image Analysis

Three-dimensional analysis was performed using the open-source software ITK-SNAP and SlicerCMF (version 4.0; http:// www.slicer.org). The original tomography files were in DICOM format and were converted into “gipl.gz” files using the open ITK-SNAP software. The 3D image analysis was performed following the steps:

1.Segmentation: construction of a volumetric label of the initial tomography (T1) of the skull base and mandible,[12] using the ITK-SNAP software (http://www.itksnap.org).

2. Head orientation: The head orientation was performed in the surface models generated in previous step. Head orientation was performed using tree planes as reference: Frankfort horizontal, midsagittal, and transporionic planes. The midsagittal plane was defined by glabella, crista galli, and basion landmarks. The Frankfort horizontal plane was defined bilaterally by the right and left porion and right and left orbitale landmarks. The transporionic plane was defined bilaterally by porion landmarks that were perpendicular to the Frankfort horizontal plane.[12]

3. Manual approximation of the initial (T1) and final (T2) scan: CBCT scans were manually approximated using the cranial base as reference in the Slicer software transformation tool.

4. Construction of a 3D mask for the cranial base registration superimposition using the ITK snap.

5. Cranial base registration: Automatic method of image registration based on voxels, using the Slicer software. These procedures used the cranial base anatomic structures as masks for reference, indicating to the software in which stable areas it should look for corresponding voxels. [16] A matrix is generated from this step and applied to T2 scan at the cephalometric points.

5. Landmarks placement:[15] In the ITK-SNAP software, cephalometric landmarks will be placed on the cranial base and mandible at T1 and T2. All landmarks used were described in Table I.

6. Generation of the 3D models in 3D Slicer.

7. Quantification: Using the module Q3DC in the Slicer software, the distances between the landmarks were calculated.

Measurements were organized into linear (in millimeters) changes for all superimpositions.

Statistical Analysis

All measurements were performed by a single observer.The Shapiro-Wilk test was used to verify normal distribution. Descriptive statistics included the mean and standard deviation (SD) of 3D landmark displacements from T1 to T2. Interphase changes were evaluated using One-sample t tests. One sample t-tests were conducted based on the mean difference between T1 values and T2 values, in order to show the effectiveness of the treatment modality. The comparative mean value for the one sample t-test was 0.0, as defined in the study's null hypothesis. Several results found a statistical significance when compared to 0.0 or no change; however, for some of these measurements the findings may not be clinically relevant. The statistical analyses were calculated using the open-source statistical software JAMOVI software (version 1.2) (https://www.jamovi.org.).

Results

Table II summarizes the changes in the condyle and glenoid fossa observed from T1 to T2. The linear changes were measured for all three superimpositions: three-dimensional (3D), anteroposterior (AP) and superior inferior (SI) displacements (mm) with treatment. (Fig. II)

The right and left condyles have few movements in the AP measurement (-0.47;0.05), where the positive number show a movement to backward and the positive number show forward movement; on the SI way they moved (0.89; 1.44), showing a little movement up; and in the 3D measurement (2.56; 2.85) we saw that the condyle moved in the spatial plane.(Fig. I)

The right and left articular fossa, the AP movements (0.21; 0.28) we saw a little forward movement; SI movements (-0.45; 0.06) show a little movement to inferior on the right side; in the 3D movement (1.86;1.65) we can observe that the articular fossa moved in the 3D planes of space.

On the right and left articular eminence, the AP movement (0.12; 0.13) show a little forward movement; for SI (-0.15; 0.12) we can observe a little movement inferior and superior; on the 3D component (1.37; 1.09) we can also see that the articular eminence moved on the 3D planes.

No intragroup statistical difference was found in the three spatial planes after treatment. Minimum displacements were observed for the condylion and glenoid fossa after treatment with MAMP therapy.

Discussion

Few studies have reported the three-dimensional remodeling of the glenoid fossa after mandibular orthopedic treatment.[7,13] Three-dimensional studies use improved technology to more accurately visualize treatment effects, while eliminating potential downsides of two-dimensional records such as patient head positioning.[12] Previous orthodontic studies and the American Board of Orthodontics used the anterior cranial base, maxillary regional, and mandibular regional landmarks to analyze growth and treatment effects through these three regions of superimposition.[12,14-17] In our study, these same standards in combination with other published methods for superimposing three-dimensional data were used. 3D assessments using cone-beam computer tomography (CBCT) have opened new horizons in the evaluation of positional changes in the condyle.[7,8, 11, 12] Reliability and reproducibility of the image analysis registration[12,15,16,18,19] and quantitative methods using the Q3DC tool[18,20,21] have been verified with previously published literature.

MAMP therapy is a new treatment option that promoted successful orthopedic changes in adolescent patients.[9,10] However, no previous study evaluated the effect of MAMP therapy in the condylar position and glenoid fossa. Minimum displacements were observed for the condylion and glenoid fossa after treatment with MAMP therapy. The symmetrical and slightly 3D remodeling of the glenoid fossa, articular eminence and articular fossa may suggest better stability of the mandibular displacement.

The right and left condylion, right and left anterior fossa, right and left articular eminence showed similar displacements in all planes of space studied (anteroposterior, superior-inferior and 3D). Therefore, bone remodeling after MAMP therapy was similar in all planes of space with a good orthopedic force acting in these areas. Previous studies showed that the reestablishment of the original condyle-fossa relationship happens due to a combination of minor bone remodeling changes as well as the mechanical drift of the condyle into its original position due to soft tissues traction. [7,20] Previous studies that evaluated the BAMP therapy effects of the condylar position and glenoid fossa found a high correlation between modeling of the anterior and posterior eminences of the glenoid fossa and displacement of the opposing condylar surfaces.[7]

The surface remodeling of the glenoid fossa can result of a combination of normal growth and the effect of the orthopedic traction. A limitation of this study is the lack of an untreated Class III sample as control group to assess and compare the normal growth changes with treatment changes. However, there would be ethical issues related to the maintaining a Class III sample untreated and with CBCT records. Another limitation of this study is the small sample size and the lack of a longitudinal follow-up. However, this study promotes new and important information regarding the displacement of the condyle and remodeling of the glenoid fossa. Futures studies should assess bigger samples and compare the longitudinal changes.

Conclusions

The MAMP therapy no produced significantly 3D displacement in the patients treated regardless of the direction of the 3D changes: anteroposterior, superior-inferior and 3D movements. Condyle show a little movement up; articular fossa little movement forward and the articular eminence movement up and forward.

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Table I. Landmarks definition.

Landmark		Definition
RCo	Condyle	Place on the on most lateral posterior and superior point of head of the right condyle.
LCo	Condyle	Place on the on most lateral posterior and superior point of head of the left condyle.
RMP	Right medial Pole	The most medial point of the right condyle
RDP	Right distal Pole	The most distal point of the right condyle
LMP	Left medial Pole	The most medial pole of the left condyle
LDP	Left distal Pole	The most distal pole of the left condyle
RAF	Right articular fossa:	The most superior and central right point of the glenoid fossa.
LAF	Left articular fossa	The most superior and central left point of the glenoid fossa.
RAE	Right articular eminence	The most inferior point on the right articular eminence
LAE	Left articular eminence	The most inferior point on the left articular eminence…

Note: All landmarks placed while being viewed in all three planes of space.
Note: All landmarks placed using the same cross-sectional view for standardization.

Table II. Condylar and articular fossa changes with treatment (One Sample t Test).

Variable	Measurement	Mean	SD	Median	P value*
RCo	AP	-0.47	1.00	-0.23	0.064
	SI	0.89	1.58	1.09	0.365
	3D	2.56	1.48	2.30	0.717
LCo	AP	0.05	1.13	0.08	0.064
	SI	1.44	1.82	0.88	0.365
	3D	2.85	1.72	2.17	0.717
RAF	AP	0.21	0.77	0.00	0.298
	SI	-0.45	1.88	0.12	0.679
	3D	1.86	1.35	1.82	0.480
LAF	AP	0.28	0.69	0.48	0.298
	SI	0.06	1.01	0.03	0.679
	3D	1.65	0.92	1.55	0.480
RAE	AP	0.12	0.46	0.00	0.904
	SI	-0.15	1.11	-0.10	0.370
	3D	1.37	0.57	1.34	0.235
LAE	AP	0.13	0.40	0.03	0.904
	SI	0.12	0.79	0.21	0.370
	3D	1.09	0.59	0.97	0.235

*Statistically significant at $P<0.05$. AP: anteroposterior; SI: superior inferior; 3D: three-dimensional.

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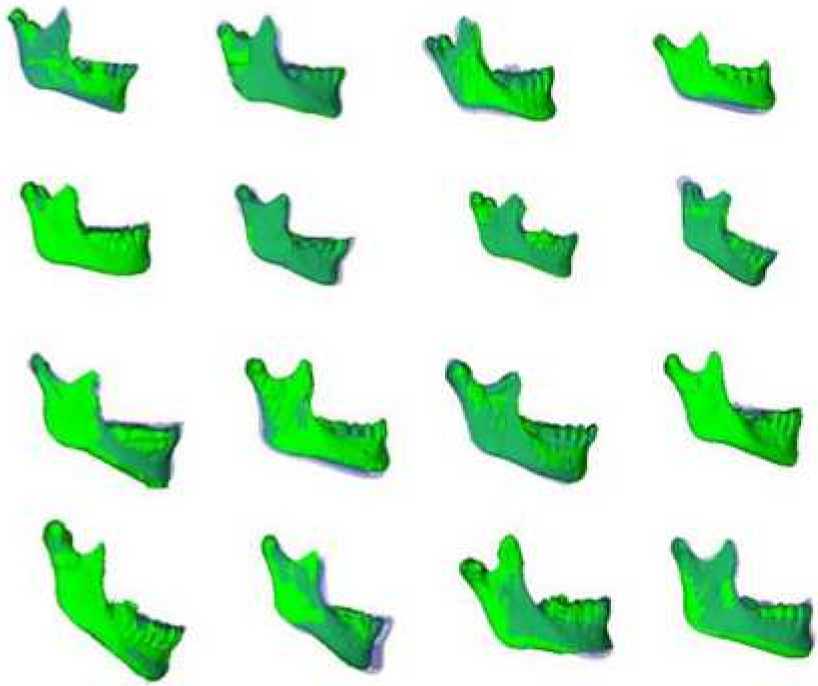

Fig I. Superimposition of pre (green color) and post-treatment mandibles (blue color) of the complete sample registered in the anterior region of the cranial base

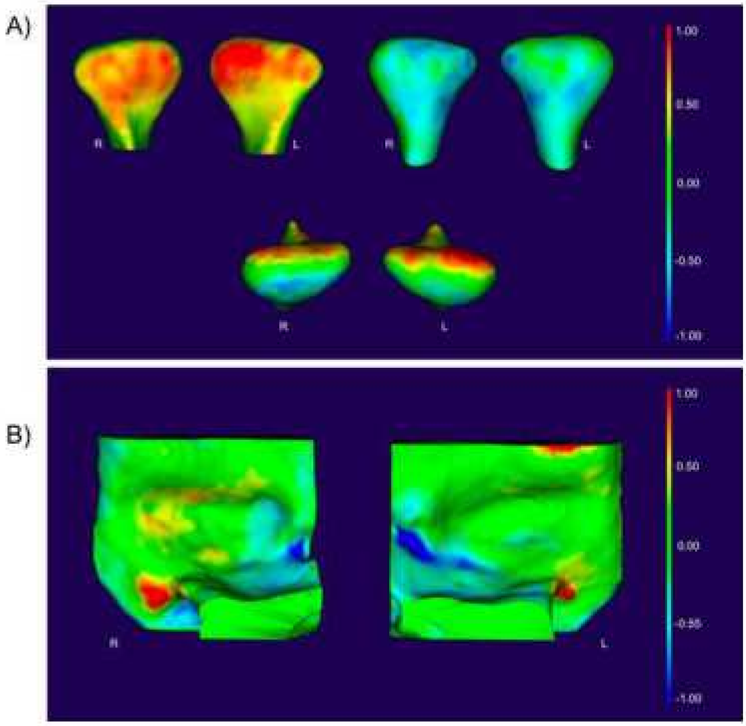

Fig II. Color maps of the glenoid fossa after registration on the anterior cranial base. The glenoid fossa moved slightly toward forward after MAMP therapy.

3 DISCUSSION

3 DISCUSSION

Few studies have reported the three-dimensional remodeling of the glenoid fossa after mandibular orthopedic treatment.[7,13] No previous studies have evaluated the 3D mandibular changes after MAMP therapy. Three-dimensional methods permit to superimpose dental records to visualize treatment effects, eliminating potential downsides of two-dimensional records such as patient head positioning.[11] In this study, the three-dimensional displacement of the mandible relative to the cranial base was assessed. Our study used a standardized method of superimposing three-dimensional data previously validated and used in other studies.[12-15,18,19]

The right and left condylion, right and left anterior fossa, right and left articular eminence showed similar displacements in all planes of space studied (anteroposterior, superior-inferior and 3D). Therefore, bone remodeling after MAMP therapy was similar in all planes of space with a good orthopedic force acting in these areas. Previous studies showed that the reestablishment of the original condyle-fossa relationship happens due to a combination of minor bone remodeling changes as well as the mechanical drift of the condyle into its original position due to soft tissues traction. [7,20] Previous studies that evaluated the BAMP therapy effects of the condylar position and glenoid fossa found a high correlation between modeling of the anterior and posterior eminences of the glenoid fossa and displacement of the opposing condylar surfaces.[7]

The surface remodeling of the glenoid fossa can result of a combination of normal growth and the effect of the orthopedic traction. A limitation of this study is the lack of an untreated Class III sample as control group to assess and compare the normal growth changes with treatment changes. However, there would be ethical issues related to the maintaining a Class III sample untreated and with CBCT records. Another limitation of this study is the small sample size and the lack of a longitudinal follow-up. However, this study promotes new and important information regarding the displacement of the condyle and remodeling of the glenoid fossa. Futures studies should assess bigger samples and compare the longitudinal changes.

The length and the anteroposterior position of the mandible remained stable during treatment (CoGn and SNB, table II). The anteroposterior displacement of Gn landmark (Table III) demonstrated a slight posterior displacement of the symphysis after MAMP therapy that was not considered clinically relevant. Although, MAMP and BAMP use Class III elastics as the active force, the direction of the force is slightly different between these therapies. In MAMP therapy, the Class III elastics are more horizontal compared to BAMP because the application point in the maxillary arch is the first molar bands. In BAMP therapy, the application point in the maxilla is approximately at the level of mucogengival junction of molars. The difference in force direction might explain the differences in the mandibular outcomes found in this study.

The Sn.GoGn angle increased by two degrees after MAMP therapy (Table IIA slight but significant increase (+0.6°) in the gonial angle (CoGo.GoGn) was also observed in our study. In addition. the Gn landmark slightly displaced downward (-0.3MM) in the SI component (Table III), following the tendency of those planes.

A slight labial tip of the mandibular incisor (II.GoGn) was found after MAMP therapy. The improvement in the maxillomandibular relationship and the correction of the negative overjet might explain the mandibular incisor labial movement. These findings are in agreement with mandibular incisor proclination observed after BAMP therapy.[7] On the other hand, the mandibular molars showed a 3D displacement similar to the mandible that means no dental effect was observed in mandibular posterior teeth once only skeletal anchorage was used during MAMP therapy.

The results from this study are limited to a short-term observation period immediately after active treatment. Future studies are necessary to evaluate the long-term stability of MAMP outcomes.

4 FINAL CONSIDERATIONS

4 FINAL CONSIDERATIONS

The right and left condylion, right and left anterior fossa, right and left articular eminence showed similar and slight displacements in all planes of space (anteroposterior, superior-inferior and 3D) after miniscrew-anchored maxillary protraction therapy. Mandibular plane rotated clockwise after MAMP therapy. The anterior region of the mandibular symphysis slightly displaced toward posterior and inferior. The mandibular length remained stable during treatment.

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REFERENCES

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APPENDIX

APPENDIX A - DECLARATION OF EXCLUSIVE USE OF THE ARTICLE 1 IN DISSERTATION/THESIS

We hereby declare that we are aware of the articles “MANDIBULAR CHANGES AFTER MINISCREW-ANCHORED MAXILLARY PROTRACTION: A 3D ANALYSIS” will be included in Dissertation of the student Luciana Trevisan Bittencourt Muniz and may not be used in other works of Graduate Programs at the Bauru School of Dentistry, University of São Paulo.

Bauru, March 2th, 2022.

Luciana Trevisan Bittencourt
Author — Signature

Jose Fernando Castanha Henriques
Author — Signature

APPENDIX B - DECLARATION OF EXCLUSIVE USE OF THE ARTICLE 2 IN DISSERTATION/THESIS

We hereby declare that we are aware of the articles "CONDYLE AND GLENOID FOSSA 3D-CHANGES AFTER MINI-SCREW ANCHORED MAXILLARY PROTRACTION" will be included in Dissertation of the student Luciana Trevisan Bittencourt Muniz and may not be used in other works of Graduate Programs at the Bauru School of Dentistry, University of São Paulo.

Bauru, March 2th, 2022.

Luciana Trevisan Bittencourt
Author — Signature

Jose Fernando Castanha Henriques
Author — Signature

ANNEX

ANNEX A – Ethics Committee approval, protocol number 5.497.991

USP - FACULDADE DE ODONTOLOGIA DE BAURU DA USP

PARECER CONSUBSTANCIADO DO CEP

DADOS DO PROJETO DE PESQUISA

Título da Pesquisa: Análise 3D das alterações mandibulares, condilares e articulares após terapia de protração maxilar ancorada em mini-implantes

Pesquisador: LUCIANA TREVISAN BITTENCOURT MUNIZ

Área Temática:

Versão: 3

CAAE: 57981622.2.0000.5417

Instituição Proponente: UNIVERSIDADE DE SAO PAULO

Patrocinador Principal: Financiamento Próprio

DADOS DO PARECER

Número do Parecer: 5.497.991

Apresentação do Projeto:

De acordo com a descrição dos pesquisadores no Projeto, a amostra será obtida a partir de um ensaio clínico randomizado (processo FAPESP n.º 2017/04141-9). Será composta por um total de 16 participantes, com idade média inicial de 10 anos e idade média final de 12 anos. Os pacientes foram tratados na clínica de Ortodontia da Faculdade de Odontologia de Bauru / USP, no período de julho de 2017 a junho de 2019. Para este estudo serão a análise das tomografias obtidas no estudo anterior.

Objetivo da Pesquisa:

Este estudo tem como objetivo avaliar tridimensionalmente as alterações no côndilo, fossa glenóide e mandíbula após a protração maxilar ancorada em mini-implantes (MAMP) em pacientes adolescentes.

Avaliação dos Riscos e Benefícios:

De acordo com os autores, riscos mínimos serão produzidos com esse estudo, tendo em vista que os pacientes já foram tratados previamente e todos os exames necessários para a análise já foram coletados. No entanto, podemos citar como possível risco a exposição de dados confidenciais do paciente. A equipe de pesquisa se compromete a manter sigilo e confidencialidade quanto aos dados dos pacientes. Nenhuma forma de identificação do participante será possível através dos

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dados obtidos com esse estudo.

Dentre os benefícios, podemos ressaltar que os resultados desse estudo contribuirão indiretamente aos participantes ao elucidar as alterações promovidas pelo tratamento de protração maxilar ancorado em mini-implantes no côndilo, fossa glenóide e mandíbula.

Comentários e Considerações sobre a Pesquisa:

Trata-se versão 3 para correção de pendências. Todas as inadequações foram corrigidas.

Considerações sobre os Termos de apresentação obrigatória:

Estão adequados.

Recomendações:

Não se aplica.

Conclusões ou Pendências e Lista de Inadequações:

Projeto aprovado sem pendências de ordem ética.

Considerações Finais a critério do CEP:

Esse projeto foi considerado APROVADO ad referendum deste CEP, com base nas normas éticas da Resolução CNS 466/12. Ao término da pesquisa o CEP-FOB/USP exige a apresentação de relatório final. Os relatórios parciais deverão estar de acordo com o cronograma e/ou parecer emitido pelo CEP. Alterações na metodologia, título, inclusão ou exclusão de autores, cronograma e quaisquer outras mudanças que sejam significativas deverão ser previamente comunicadas a este CEP sob risco de não aprovação do relatório final. Quando da apresentação deste, deverão ser incluídos todos os TCLEs e/ou termos de doação assinados e rubricados, se pertinentes.

Este parecer foi elaborado baseado nos documentos abaixo relacionados:

Tipo Documento	Arquivo	Postagem	Autor	Situação
Informações Básicas do Projeto	PB_INFORMAÇÕES_BÁSICAS_DO_PROJETO_1880849.pdf	21/06/2022 13:23:21		Aceito
Folha de Rosto	folhaDeRostoass.pdf	21/06/2022 13:22:56	LUCIANA TREVISAN BITTENCOURT MUNIZ	Aceito
Outros	CEP_Cartaresposta.pdf	09/06/2022 21:22:32	LUCIANA TREVISAN BITTENCOURT MUNIZ	Aceito
Projeto Detalhado / Brochura Investigador	Projeto_CEP_revisado.pdf	09/06/2022 21:21:28	LUCIANA TREVISAN BITTENCOURT MUNIZ	Aceito

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Continuação do Parecer: [illegible]

Outros	FE_CEP.pdf	10/05/2022 14:46:41	LUCIANA TREVISAN BITTENCOURT MUNIZ	Aceito
Declaração de Instituição e Infraestrutura	Comite_etica_assinado_Luciana.pdf	02/05/2022 09:07:55	Juliana Fraga Soares Bombonatti	Aceito
Recurso Anexado pelo Pesquisador	2cep_docs_proj_pesquisa_termo_de_aquiescenciaEXTERNO.pdf	17/04/2022 20:00:21	LUCIANA TREVISAN BITTENCOURT MUNIZ	Aceito
Outros	Check_listCEP_2019.pdf	11/03/2022 21:28:47	LUCIANA TREVISAN BITTENCOURT MUNIZ	Aceito
Solicitação Assinada pelo Pesquisador Responsável	DeclaracaoCompromissoPesquisadorResultadosPesquisa.pdf	11/03/2022 21:25:49	LUCIANA TREVISAN BITTENCOURT MUNIZ	Aceito
Declaração de Instituição e Infraestrutura	cep_docs_proj_pesquisa_carta_de_encaminhamento_termo_de_aquiescencia.pdf	11/03/2022 21:24:34	LUCIANA TREVISAN BITTENCOURT MUNIZ	Aceito

Situação do Parecer:
Aprovado

Necessita Apreciação da CONEP:
Não

BAURU, 29 de Junho de 2022

Assinado por:
Juliana Fraga Soares Bombonatti
(Coordenador(a))

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